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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/825,219	04/16/2004	Alfons Bosman	BJS-2551-149	7081

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EXAMINER

BOESEN, AGNIESZKA

ART UNIT	PAPER NUMBER
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1648

MAIL DATE	DELIVERY MODE
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07/27/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/825,219	Applicant(s) BOSMAN ET AL.	
	Examiner Agnieszka Boesen	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 April 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 12-33 is/are pending in the application.
- 4a) Of the above claim(s) 21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 12-20 and 22-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>6/11/2007</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

The Amendment filed April 23, 2007 in response to the Office Action of January 22, 2007 is acknowledged and has been entered. Claims 12-14, 16-23 have been amended. New claims 24-33 have been added. Claim 21 is withdrawn. Claims 12-20, and 22-33 are under examination.

Information Disclosure Statement

The Information Disclosure Statements submitted June 11, 2007 has been considered and the copies are attached to this Office Action.

Foreign Priority

The certified copy of the foreign priority document EP 99870225.2 has been received. The foreign priority document EP 94870132 received by the Patent Office in the parent application 08/612,973 was not found in the file of the parent application 08/612,973, which is US Patent 6,150,134. Applicant is requested to provide the priority document. Applicant states that the above priority document will be provided under separate cover.

Claim Rejections - 35 USC § 112

Rejection of claims 17-19 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is **withdrawn** in view of Applicants' arguments.

Rejection of claims 12-22 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is **withdrawn** in view of Applicants' amendment.

Claim Rejections - 35 USC § 102

Rejection of claims 16, 17, 20, 22 under 35 U.S.C. 102(b) as being anticipated by Grakoui et al. (Journal of Virology, 1993) is **withdrawn** in view of Applicants' arguments.

Rejection of claims 16, 17, 20, 22 under 35 U.S.C. 102(e) as being anticipated by Watanabe et al., (US Patent 5,610,009) is **withdrawn** in view of Applicants' arguments.

New Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 12-20, 22-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maertens (WO 96/04385, IDS of 8/25/2007) in view of Hofstaetter et al. (Vax Sang. Vol. 45, p. 155-165, IDS of 6/11/2007).

Claims are drawn to an isolated HCV envelope protein E1s or E1p, or a functionally equivalent part thereof comprising at least one Cys amino acid, which is reversibly protected. The said functionally equivalent part comprises at least two Cys amino acids in the configuration Cys-X1-X2-Cys, wherein X1 is Val, Leu or Ile, and X2 is Pro. The claims are also drawn to a method of raising antibodies that specifically recognize HCV E1 protein comprising administering the isolated HCV envelope protein to a mammal.

Maertens teaches purified HCV E1 proteins, and a peptide comprising the presently claimed motif Cys-X1-X2-Cys, specifically Cys-Val-Pro-Cys at amino acids 226-229 (see e.g.,

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Table 3, E1-37, 217-236, SEQ ID NO: 60). Maertens teaches a method of raising antibodies that specifically recognize HCV E1 protein comprising administering the isolated HCV envelope protein to a mammal (see page 54-57).

Maertens teaches the importance of cysteine residues involved in disulfide bonding for the purpose of maintaining the structure of conformational epitopes (page 4, lines 14-17, e.g.). Maertens teaches purification procedure for HCV E1 proteins comprising, reversibly or irreversibly blocking free thiol groups within the cysteines on the protein, through the process of reduction or oxidation (see, e.g., the Abstract; page 12, line 31-page 16, line 24). Maertens does not expressly teach sulfonation.

Hofstaetter teaches reversible sulfonation of cysteine residues of antibodies (see the entire document, particularly materials and Methods). Hofstaetter teaches that sulfonation of cysteine residues of antibodies for intravenous use results in loss of the ability of the antibody to react and activate the complement system with the concomitant generation and release of mediators causing inflammatory and anaphylactic reactions. Thus preparations comprising sulfonated proteins comprise lower risk of inducing an anaphylactic shock (see Discussion page 164). Hofstaetter teaches that sulfonation has a unique advantage of being the only existing chemical modification that is reversible in vitro and in vivo (see Discussion page 163).

Thus in view of Hofstaetters' teachings, it would have been obvious to sulfonate cysteine residues of proteins designed for in vivo use. One would have been motivated to sulfonate cysteine residues of Maertens' HCV proteins, because Maertens teaches the importance of cysteine residues involved in disulfide bonding for the purpose of maintaining the structure of conformational epitopes and because Hofstaetter teaches that sulfonation has a unique advantage

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of being the only existing chemical modification that is reversible in vitro and in vivo and that sulfinated proteins have lower risk of causing anaphylactic shock when administered to an individual.

One would have had a reasonable expectation of success to provide a composition comprising HCV proteins wherein the cysteine residues are reversibly sulfonated because sulfonation is a long-known method of modifying disulfide bonds as taught by Hofstaetter (see page 163).

Thus the present invention would have been *prima facie* obvious to the skilled artisan at the time when the invention was made.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnieszka Boesen whose telephone number is 571-272-8035. The examiner can normally be reached on 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Agnieszka Boesen, Ph.D.

/Stacy B. Chen/ 7-23-2007
Primary Examiner, TC1600